2 expressly identify Dpr protein and Dps protein as "ferritin-like spherical proteins"; page 5, lines 8-9 define "an apoferritin-like particle" to consist of a "ferritin-like particle deficient of molecules in the cavity inside of the protein; and page 5, line 12 states "Examples of ferritin-like particles have been given above." One of ordinary skill in the art would understand the inventors had possession of the presently-claimed invention from this disclosure.

A person skilled in the art would easily recognize the application as a whole and especially the examples all relate to incorporating binding moieties into subunits of apoferritin (and apoferritin-like particles such as Dpr and Dps protein particles) by genetic fusion. All the binding moieties of the disclosed embodiments of the invention are genetically fused into subunits of the apoferritin nanoparticle. Thus, Examples 8-11 illustrate the production of genetically fused subunits having genes expressing protein G (Example 8), scFv fragment (Example 9), calmoudulin binding peptide (Example 10) and biotinylated peptide (Example 11). Ferritin-based nanoparticles expressing these binding moieties on their surface were prepared in Example 1. One of ordinary skill in the art would recognize the inventors had possession of the

presently-claimed nanoparticle as of the filing date of this application.

Reconsideration and withdrawal of the 35 U.S.C. § 112, first paragraph, rejection of claims 26-38 are respectfully requested.

The 35 U.S.C. § 102(b) rejection of claims 26, 27, 29 and 36-38 over U.S. Patent No. 4,959,306 to Kameda et al. is traversed. The claimed nanoparticle is a recombinant apoferritin particle (or a recombinant Dpr protein particle or recombinant Dps protein particle) in which at least first binding moieties are genetically fused to protein and/or peptide subunits. Importantly, genetic fusion produces a continuous polypeptide chain of the subunit in which the first binding moieties are incorporated. Accordingly, all corresponding subunits of the apoferritin where a first binding moiety has been genetically fused are identical to one another, i.e. the binding moieties are each located at the same place in the subunit's polypeptide chain. See the attached Rule 132 Declaration, particularly paragraph Nos. 9-12.

Kameda et al. fails to disclose the claimed recombinant nanoparticle. Instead, Kameda et al. discloses ferritin particles having chemically bound binding moieties, e.g. a polypeptide of a ferritin subunit (see Fig 1B and Example 1 of Kameda et al.).

Importantly, the binding moieties of the subunits of the ferritin of Kameda et al. are distributed to random locations of the polypeptide chain susceptible to attachment of the chemical linker, which results in great variation of the nanoparticles of Kameda et al. Consequently, it is not practical to prepare uniform nanoparticles, consisting of identical subunits, using the Kameda et al. method. See paragraph Nos. 7 and 11 of the enclosed Declaration.

In short, Kameda et al.'s chemically synthesized particle is structurally not the same particle as the claimed recombinant nanoparticle produced by genetic fusion. Reconsideration and withdrawal of the anticipation rejection of claims 26, 27, 29 and 36-38 over Kameda et al. are respectfully requested.

The 35 U.S.C. § 103(a) rejection of claim 30 over Kameda et al. in view of U.S. Patent No. 6,713,274 to Bertozzi et al. is traversed. As discussed above, the claimed nanoparticle is a recombinant apoferritin particle, a recombinant Dpr protein particle or a recombinant Dps protein particle, in which at least a first binding moiety has been genetically fused to protein and/or peptide subunits. A structural feature of the claimed nanoparticle is that all corresponding subunits of the apoferritin where a first

binding moiety has been genetically fused are identical to one another, i.e. the binding moieties are each located at the same place in the subunit's polypeptide chain.

The cited combination of references fails to raise a prima facie case of obviousness against claim 30 because neither reference discloses or suggests the genetically fused, uniform subunit feature of the claimed nanoparticle. As discussed above, Kameda et al. chemically binds its binding moieties to ferritin subunits, which produces random distribution of the binding moieties on the polypeptide chain. Bertozzi et al. is cited to show fluorescein, luciferase and ^{124}Eu may be used as a detectable label for detection of antibody binding, and fails to disclose or suggest modifying the Kameda et al. nanoparticle by preparing it using genetic fusion. Reconsideration and withdrawal of the obviousness rejection of claim 30 over Kameda et al. in view of Bertozzi et al. are earnestly requested.

The 35 U.S.C. § 103(a) rejection of claim 31 over Kameda et al. in view of U.S. Patent Publication 2003/0124586 to Griffiths et al. is traversed. A structural feature of the claimed recombinant nanoparticle is that all corresponding subunits of the apoferritin

where a first binding moiety has been genetically fused are identical to one another.

The cited combination of references fails to raise a prima facie case of obviousness because neither reference discloses or suggests the genetically fused, uniform subunit feature of the claimed nanoparticle. Kameda et al. chemically binds its binding moieties to ferritin subunits, which produces random distribution of the binding moieties on the polypeptide chain. Griffiths et al. chemically binds a biotinylated DNA fragment to a complex of avidin and apoferritin. One of ordinary skill in the art is given no disclosure or suggestion to modify Kameda et al.'s nanoparticle by preparing it using genetic fusion. Reconsideration and withdrawal of the obviousness rejection of claim 31 are respectfully requested.

The 35 U.S.C. § 103(a) rejection of claims 28 and 32 over Kameda et al. in view of U.S. Patent No. 6,599,331 to Chandler et al. is traversed. A structural feature of the claimed recombinant nanoparticle is that all corresponding subunits of the apoferritin where a first binding moiety has been genetically fused are identical to one another.

The cited combination of references fails to raise a prima facie case of obviousness against the claimed nanoparticle because neither reference discloses or suggests the genetically fused, uniform subunit feature of the claimed nanoparticle. Kameda et al. chemically binds its binding moieties to ferritin subunits, which produces random distribution of the binding moieties on the polypeptide chain. Chandler et al. is cited to show the use of protein A as a binding moiety. However, Chandler et al. provides no motivation to modify Kameda et al.'s nanoparticle by preparing it using genetic fusion. Reconsideration and withdrawal of the obviousness rejection of claims 28 and 32 are respectfully requested.

The 35 U.S.C. § 103(a) rejection of claims 33, 35 and 36 over Kameda et al. in view of U.S. Patent No. 6,537,760 to Bergmann et al. is traversed. A structural feature of the claimed recombinant nanoparticle is that all corresponding subunits of the apoferritin where a first binding moiety has been genetically fused are identical to one another.

The cited combination of references fails to raise a prima facie case of obviousness against the claimed nanoparticle because neither reference discloses or suggests the genetically fused,

uniform subunit feature of the claimed nanoparticle. Kameda et al. chemically binds its binding moieties to ferritin subunits, which produces random distribution of the binding moieties on the polypeptide chain. Bergmann et al. discloses a competitive receptor binding assay for detecting TSH-receptor auto-antibodies. One of ordinary skill in the art is given no suggestion or motivation to prepare Kameda et al.'s nanoparticle by genetic fusing a first binding moiety and a ferritin sub-unit. Reconsideration and withdrawal of the obviousness rejection of claims 33, 35 and 36 over Kameda et al. in view of Bergmann et al. are respectfully requested.

The 35 U.S.C. § 103(a) rejection of claim 34 over Kameda et al. in view of U.S. Patent Publication No. US 2003/0077578 to Oon et al. is traversed. A structural feature of the claimed recombinant nanoparticle is that all corresponding subunits of the apoferritin where a first binding moiety has been genetically fused are identical to one another.

The cited combination of references fails to raise a prima facie case of obviousness against the claimed nanoparticle because neither reference discloses or suggests the genetically fused, uniform subunit feature of the claimed nanoparticle. Kameda et al.

chemically binds its binding moieties to ferritin subunits, which produces random distribution of the binding moieties on the polypeptide chain. Oon et al. discloses a nucleic acid based assay for detection of a virus pathogen such as hepatitis B virus. One of ordinary skill in the art is given no suggestion or motivation to prepare Kameda et al.'s nanoparticle by genetic fusing a first binding moiety and a ferritin sub-unit. Reconsideration and withdrawal of the obviousness rejection of claim 34 are respectfully requested.

A Supplemental Information Disclosure Statement which submits the references cited in the Rule 132 declaration is attached.

It is believed this application is in condition for allowance. Reconsideration and withdrawal of all rejections of claims 26-38, and issuance of a Notice of Allowance directed to these claims, are earnestly requested. The Examiner is urged to telephone the undersigned should she believe any further action is required for allowance.

The fees for the extension of time and the RCE are being paid electronically today. It is not believed any additional fee is required for entry and consideration of this Amendment.

Nevertheless, the Commissioner is authorized to charge Deposit Account No. 50-1258 in the amount of any such required fee.

Respectfully submitted,

/James C. Lydon/

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Enclosures:
- Petition for Extension of Time
- Request for Continued Examination
- Declaration Pursuant to 37 C.F.R. § 1.132
- Supplemental Information Disclosure Statement